The Wheelchair Thrombosis Syndrome

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Financial support: Support from Fairview Developmental Center (Department of Developmental Services, State of California). Opinions expressed herein are those of the authors only.

This case was presented at the 29th Quarterly Grand Rounds at Fairview Developmental Center on November 2, 2005.

Objective: To report a case of deep vein thrombosis (DVT) related to prolonged wheelchair use.

Case Report: A 48-year-old patient with spastic quadriplegia usually spent 10–12 hours daily in a wheelchair. He suddenly developed marked swelling of his right foot, leg and thigh. His plasma D-dimer level was 1,030 (normal <500) ng/ml. A duplex ultrasound revealed common femoral vein thrombosis. He was hospitalized and anticoagulated; his extremity swelling decreased considerably by day 45. Hypercoagulability work-up disclosed previously subclinical mild elevation of serum cardiolipin immunoglobulin G (antiphospholipid syndrome). This patient will receive long-term anticoagulation.

Conclusion: Prolonged sitting in wheelchair may cause DVT. To enhance public recognition of this avoidable risk, we propose the term "wheelchair thrombosis syndrome."

Key words: deep vein thrombosis ■ wheelchair ■ mental retardation ■ quadriplegia ■ antiphospholipid syndrome

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People with mental retardation and spastic quadriplegia usually spend their entire life in a wheelchair or bed. Such immobility should predispose them to deep vein thrombosis (DVT).[1-6] They may also concurrently experience other prothrombotic influences from the Virchow's thrombosis triad (venous stasis, endothelial damage, hypercoagulability).[1] Although they generally receive no DVT prophylaxis, DVT is reportedly rare in them.[7] In the only published study for this population, no DVT case was diagnosed during 18 years among 57 such residents (1,026 patient years).[7] However, DVT cases were probably missed in that study because of the lack of objective testing and the inherent problem of suboptimal case identification in retrospective research. Clinical diagnosis of DVT without ultrasound is incorrect in 50% of cases.[1,8] Thus, previously undiagnosed thigh DVT was identified by ultrasound in 11% of 709 brain injury patients.[9] Even ultrasound may miss some cases.[10] Nonrecognition of DVT is even more likely in quadriplegics with mental retardation because their inability to ambulate may mask pain and limping, and concomitant aphasia may prevent verbalization of symptoms. We present a case of DVT related to prolonged wheelchair use in such a patient.

CASE REPORT

"John," a 48-year-old resident of a developmental center, had a normal gestation, birth and childhood. At age 9, he required a craniotomy for an intracranial hemorrhage from an automobile accident. Subsequently, he developed hydrocephalus (necessitating a ventriculoatrial shunt), encephalomalacia, profound mental retardation (Binet Kuhlman intelligence quotient: 12), tonic clonic epilepsy, dysphagia, dysphasia, contractures and spastic quadriplegia.

John's weight was 194 lbs. (88 kg), height 71" (180 cm) and body mass index 27 kg/m^2 (overweight, but not obese). He received daily 1.4 g carbamazepine and 180 mg phenobarbital for tonic-clonic epilepsy (seizure frequency 1–2 per year). He had no other ongoing clinical problem. He was nonverbal, nonambulatory and dependent on caregivers for all activities of daily living. He had negligible active motion in any extremity. An electric lift was used for transferring him between his bed and chair. His wheelchair was equipped with a gel cushion, antitipping and tilt-in-space mechanisms, seat belt, foot bucket and hand rims. The seat edge touched his posterior thighs but caused no significant compression. On a typical day, John sat in his wheelchair from 7 am to 1 pm (six hours) for breakfast, lunch and group room activities (music, television, developmental training). He rested in his bed between 1 pm and 3 pm. Then, he again sat in his wheelchair until 8 pm (five hours). While sitting, his knees usually had >45° flexion. He slept from 8 pm to 7 am.

One day, an astute caregiver noted sudden swelling of John's right foot. This swelling progressively, rapidly and considerably worsened to involve his entire ipsilateral leg, thigh and buttock (Table 1). There was no fever, bruise, increased warmth, tenderness, crepitus, erythema, varicose vein, superficial vein congestion, palpable venous cord or sign of chronic venous insufficiency. The extremity was rather pale, suggesting phlegmasia alba dolens (compression of capillaries due to increased interstitial pressure and reflex arterial spasm). Pedal pulses were intact. Response to passive dorsiflexion of the ankle (Homans' sign for calf vein thrombosis) was a nonchalant grimace. John was hospitalized. Results were normal for blood count, urinalysis, serum chemistry and thyroid panels, and serum carbamazepine and phenobarbital levels. His plasma D-dimer level was elevated to 1,030 (normal <500) ng/ml, suggesting DVT. On duplex ultrasound, the common femoral vein was not compressible. The superficial femoral and the popliteal veins could not be visualized due to John's habitus. An electrocardiogram revealed a PR interval of 204 (normal 120–200) ms.

To prevent dislodgement of the newly formed thrombus, John was put on strict bed rest for seven days—the time thrombi usually take to firmly adhere to the vessel endothelium. Early ambulation can dislodge the new clot, while sitting raises venous pressure and aggravates edema. John's feet were elevated 20° above the level of the heart, and elastic stockings were applied to augment venous return, to prevent the formation of new thrombi, and to reduce edema and blood pooling in the venous sinuses.

John was given anticoagulants to facilitate natural fibrinolysis of the original thrombus and prevent new thrombogenesis. Warfarin, a vitamin-K antagonist, is the only commercially available oral anticoagulant. However, it takes 3–4 days for a full therapeutic effect and may cause a biochemical paradox (initial hypercoagulability by inhibiting the vitamin K-dependent synthesis of natural anticoagulants—proteins C and S).[1,8] Heparin acts rapidly, but requires intravenous administration, has an unpredictable dose-response necessitating monitoring with active partial thromboplastin time, and may cause bleeding or thrombocytopenia. Subcutaneous low-molecular-weight heparins (such as enoxaparin, dalteparin, tinzaparin) act rapidly, and their predictable dose response eliminates the need for monitoring with coagulation tests. Therefore, John was given enoxaparin 80 mg twice daily, with concomitant warfarin 5 mg daily. Enoxaparin was continued for five days until warfarin had prolonged the prothrombin time to an international normalized ratio of 2–3 (the risk of bleeding with this regimen is an acceptable 4%).[1,8] Such treatment led to considerable reduction of John's extremity edema within 45 days, although some swelling remained (Table 1).

Hypercoagulability testing revealed that John had an elevated level of cardiolipin immunoglobulin G (by enzyme linked immunosorbent assay) on two separate occasions >6 weeks apart. John had negative tests for antinuclear antibody, rheumatoid factor, syphilis, anti-DNA, lupus anticoagulant and Russell's viper venom. John had no additional prothrombotic factor from the Virchow's thrombosis triad (Table 2).

After the acute phase, our treatment goals were to prevent recurrent thromboembolism, allow the development of venous collaterals and prevent postthrombotic syndrome (from venous valve destruction during recanalization of the thrombosed veins). In most cases of first DVT episode, 3–6 months of anticoagulation is adequate. The incidence of thromboembolism in anticoagulated patients is 2% compared to 47% in untreated patients.[1,8] Since John is predisposed to DVT due to immobility and antiphospholipid syndrome, he will receive longer, probably lifelong, anticoagulation and nonpharmacologic DVT prophylaxis. Should he still have thrombotic events, he will require a prophylactic inferior vena caval filter to prevent pulmonary embolism (Table 3).

DISCUSSION

John's DVT was primarily caused by prolonged sitting in a wheelchair. Immobility inactivates the calf-pump, reduces blood velocity and promotes venous stasis.[1,8] Venous pressure is equivalent to the height of a hydrostatic column extending from the heart to the calf veins. When supine, such pressure is 0, but it rises to 50–90 cm of water while sitting. Longer legs and the resultant increased venous pressure while sitting are probably the reason why tall men like John have more DVT.[11] Prolonged sitting with bent knees in confined

Table 1. Girth measurements at various levels of patient's lower extremities

Site of Measurement	Girth of Healthy Extremity	Girth of Affected Extremity (and Increase over Healthy Extremity), Days after Diagnosis	
		0 days	45 days
Thigh, 10 cm above superior pole of patella	43.5 cm	53.2 (+9.7) cm	46.5 (+3) cm
Calf, 10 cm below tibial tuberosity	27.8 cm	37 (+9.2) cm	30.0 (+2.2) cm

The statistical significance of the observed differences could not be determined because the sample consisted of only one subject. However, clinically the changes were obvious—marked swelling of the right lower extremity on day 0, with considerable improvement by day 45. Girths of the unaffected left lower extremity were essentially identical on both days.

spaces, as in airplanes (the economy class syndrome), theaters or automobiles is particularly dangerous because of such leg dependency in a stationary position.[1,8,12-15] During the London "blitz," fatal thromboembolism developed after just a few hours of sitting still in air raid shelters.[15] Clearly, DVT risk is greater while sitting than while lying in bed. Most healthy people do not develop DVT because they usually move their legs while sitting and interrupt severe prolonged venous stasis. However, most wheelchair users are unable to move their legs and therefore become predisposed to DVT. Although as many as 1.4 million Americans regularly use a wheelchair (www.pascenter.org/disabilitydata/disability/2_2.php, accessed 12/08/05), this wheelchair-associated DVT risk remains underappreciated. A PubMed search for this condition identified no citation (www.ncbi.nlm.mih.gov/entrez, searched 03/15/06). To enhance public recognition of this avoidable risk, we propose the term "wheelchair thrombosis syndrome."

The extent of extremity swelling yields a clue to the level of venous obstruction: thigh with common femoral or external iliac, leg with femoral, and foot with leg vein thrombosis.[1,8] In John's case, the swelling first appeared in his foot and progressively extended proximally to involve the entire right lower extremity. This sequence suggests thrombosis of the calf veins initially with propagation to the popliteal, superficial femoral, common femoral and the external iliac veins. However, John's ultrasound revealed thrombosis of only the common femoral vein. This discordant result may be because ultrasound is not sufficiently sensitive for the smaller calf veins and the deeper external iliac vein; it is also operator dependent, requiring localization and compressibility testing of each vein by a handheld linear probe.[1,8] The residual swelling of John's extremity probably reflects poor venous return due to inadequate development of collaterals, incomplete reendothelialization of the thrombosed veins, and increased retrograde venous pressure from destruction of venous valves during thrombolysis.[1,8]

Proximal DVT is a potentially life-threatening entity, with the development of pulmonary embolism in 10% and chronic venous insufficiency in 25% cases.[1,8] It must be promptly differentiated from two other serious diseases that produce a painful swollen leg—cellulitis (hot, red swelling) and necrotizing fasciitis (septic patient with bullae, crepitus and evidence of rhabdomyolysis or disseminated intravascular coagulation).[1] Less

Table 2. Results of investigation for prothrombotic factors

Test	Patient Value	Reference Normal	Unit
Primary Hypercoagulability			
Prothrombotic Factors			
Antiphospholipid antibody			
Cardiolipin Immunoglobulin G	12	0–6	GPL
Cardiolipin immunoglobulin M	8	0–14	MPL
Factor V Leiden (activated protein C resistance, factor Va)	Absent	Absent	
Prothrombin 20210A (mutant)	Wild	Wild	
Fibrinogen	403	156–400	mg/ml
Homocysteine, serum	4	5–15	uM/L
Homocysteine, urine	42	0–53	mg/L
Plasminogen activity	65	70–113	%
Antithrombotic Factors			
Antithrombin III	106	88–132	%
Proteins C and S levels could not be determined accurately because the patient was taking warfarin (which inhibits their synthesis)			
Hypercoagulability due to Cancer			
Alpha fetoprotein	1.8	0–5.0	ng/ml
Carcinoembryonic antigen	1.7	0–3.1	ng/dl
Prostate specific antigen	0.4	0–4	mcg/L
Plasma and urine protein electrophoresis (multiple myeloma)	No paraproteins	No paraproteins	
Blood count for polycythemia or cytopenia	Normal	Normal	
Hemoccult, stool (gastrointestinal cancer)	Negative	Negative	
Miscellaneous			
Venous stasis (obesity, congestive heart failure)	Absent	Absent	
Endothelial damage (trauma, surgery, vasculitis)	Absent	Absent	
Hypercoagulability (phenylketonuria, cancer, smoking, mucopolysaccharidosis, polycythemia, nephrotic syndrome, diabetes mellitus, prior thrombosis, sex hormones, systemic lupus erythematosus)	Absent	Absent	

serious conditions for differential diagnosis include muscle strain or tear, lymphangitis, leg swelling in a paralyzed limb and venous reflux.[1,8]

The Wells clinical prediction guide is useful in quantifying the pretest DVT probability by incorporating risk factors, clinical signs and alternative diagnoses.[16] However, even such assessment may yield probabilities neither sufficiently high to give anticoagulants nor low enough to withhold treatment. Plasma D-dimer (a fibrinolysis product) level is useful in this context. A normal D-dimer level virtually excludes DVT, while a level >500 ng/ml is 99% sensitive for it.[17,18] However, with only 33% specificity, it can often be false positive in patients with malignancy or surgery.[8] Venous Doppler ultrasound is the noninvasive procedure of choice for confirming DVT.[1,8] A negative ultrasound followed by a negative retest after one week virtually excludes DVT. For patients strongly suspected of having DVT but with equivocal ultrasound and D-dimer results, ascending magnetic resonance venography may clear the diagnosis.[1,8]

John had a mild elevation of serum cardiolipin immunoglobulin G, suggesting antiphospholipid syndrome.[19] Such patients may have recurrent arterial or venous thrombosis, fetal loss, thrombocytopenia or false positive syphilis tests.[1,8,19] This syndrome may be secondary to systemic lupus erythematosus, but John had no evidence of the latter. Some such patients also have cardiomyopathy,[20] but John had no cardiac symptoms other than borderline first-degree atrioventricular block. Anticardiolipin G has a greater association with thrombosis compared to the M and A isotypes. The cardiolipin IgG level varies with time, and diagnosis requires an abnormal level on two occasions >6 weeks apart. A cardiolipin IgG level >50 GPL indicates a high thrombosis risk with catastrophic vascular occlusions in multiple sites simultaneously. To prevent new clotting

Table 3. Prevention of deep vein thrombosis among people with mental retardation and spastic quadriplegia

Prophylactic Measure	Physiologic Basis
Primary Prevention	
Hourly ankle–knee flexion-extension exercises (facilitate with a footboard), intermittent vasopneumatic compression of legs	Prevent stasis in the large venous sinuses of the leg muscles (gastrocnemius and soleus), facilitate venous return (replaces the calf-pump).
Elastic stockings	Prevent stasis in the venous sinuses. Facilitate venous return. Watch for skin care and wear problems in patients with contractures and inability to put them on. It may be difficult to put on thigh-length stockings in such patients. Skin may become soiled with feces or urine underneath the stocking. Poorly worn stockings may distend proximal veins and cause edema.
Elevate foot end of bed 20° above heart level	Prevents stasis and facilitates venous return
Limit continuous sitting to 1–2 hours, limit knee flexion to <45° while seated.	Interrupts prolonged stasis and venous pressure in leg veins, reduces edema, averts the development of varicose veins
Avoid sex steroids (estrogen for menstrual disorders, megestrol for anorexia)	Reduce all avoidable prothrombotic factors
Secondary Prevention (Early Diagnosis)	
Use the Wells Clinical Prediction Guide to assess DVT probability. Liberally order objective tests as morbidity is high from missed diagnosis or unnecessary treatment.	
For all patients with an unexplained leg swelling, determine plasma D-dimer. If normal, it virtually excludes DVT. If DVT is still suspected, order a duplex venous ultrasound. If normal but DVT is still suspected, repeat the duplex ultrasound after one week; if still negative, DVT is ruled out.	
If plasma D-dimer is elevated, do a duplex venous ultrasound to confirm DVT, since the plasma D-dimer test can be false positive.	
Screen all DVT patients for hypercoagulability to determine appropriate duration of anticoagulation.	

events, antiphospholipid patients require long-term anticoagulation with a higher target prothrombin time international normalized ratio of 3–3.5.[8,19]

DVT is reportedly rare in people with mental retardation.[7] If true, it may be because such patients acquire quadriplegia during childhood. The resultant long-term spasticity may considerably shrink the legs' venous sinuses and prevent venous stasis. In contrast, the bedridden elderly in nursing homes remain predisposed to DVT 10 times more (1% per year) than the general population because they acquire spasticity in their old age.[8]

This case illustrates three points. First, DVT may develop in patients with mental retardation and spastic quadriplegia. Second, when such patients develop DVT, they should be screened for hypercoagulability to determine the optimal duration of anticoagulation; their DVT should not be reflexively assumed to be merely due to immobility. Third, prolonged wheelchair use by people with limited mobility is particularly risky. Of our 600-some residents, almost 25% have disabilities that interfere with independent ambulation. Although DVT is rarely diagnosed in our institution, our occasional sudden deaths may represent pulmonary embolism from DVT. Prospective studies are warranted to determine the true DVT incidence and to develop effective preventive strategies in this vulnerable population. Prevention of new morbidity and disability is a time-honored and highly coveted goal in the care of people with considerable preexisting disability. DVT prevention may be an important leg of this marathon.

ACKNOWLEDGEMENT

The authors are grateful to Barbara Rycroft for library services; Anita Iannucci, PhD (University of California, Irvine) for statistical consultation; and the peer reviewers of this manuscript for their kind and thoughtful remarks.

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